

Exhibit B:
Copy of Lab Notebook LB101
pages 125-135

Temperature Study (D067 v01)

Aim. To determine the budesonide content and related substances present in heat stressed samples of budesonide concentrations following D067 v01.

Protocol. D067 v01

Methods. DTM003 v02.

Spec. N/A.

Analyst. PLAMR

Analyzed. [REDACTED]

Millennium Project. NPD2-Budesonide.

Sample Set. 09-0018

Acquisition method. DTM003 Ver02

Process method. DTM003

Reporting method. DTM003 assay.

Sequence of Inj. Refer to raw data.

VOID

Temp Study.Concentrate Prep.

Concentrate A (37 mg/ml) - LB137 pg 7. Actual Conc 37.6610 mg/ml.

Conc B (75 mg/ml) - LB137 pg 7. Actual Conc 75.1422 mg/ml.

Conc C (75 mg/ml) - LB137 pg 7. Actual Conc 75.0982 mg/ml.

Conc D (150 mg/ml) - LB137 pg 7. Actual Conc 150.1612 mg/ml.

NOTE The above concentrates were separated and heated as below.

Treatment of concentrates.

A1 + A2 - Controls

A3 + A4 - Heated at 110°C for 120 mins

A5 + A6 - Heated at 121°C for 20 mins

A7 + A8 - Heated at 121°C for 30 mins.

B1 + B2 - Controls

B3 + B4 - Heated at 110°C for 120 mins

B5 + B6 - Heated at 121°C for 20 mins

B7 + B8 - Heated at 121°C for 30 mins

C1 + C2 - Controls

C3 + C4 - Heated at 121°C for 20 mins

D1 + D2 - Controls

D3 + D4 - Heated at 121°C for 20 mins.

Temp StudyStandard Preparation

Wk Std A. SS. [REDACTED].001.PL. SS042 pg 82.
10.01mg budesonide in stock std (99.8%)

Wk Std B. SS. [REDACTED].002.PL. SS042 pg 82
10.07mg budesonide in stock std (99.8%)

LoQ Solution. SS. [REDACTED].004.PL.
[REDACTED].007.PL. SS042 pg 58
PL. [REDACTED].

Sample Solutions

SS. [REDACTED].003-02G.PL. SS.042 pg 85.

Placebo. SS. [REDACTED].005.PL. SS042 pg 57

Brand Sample. SS. [REDACTED].006.PL. SS042 pg 57.

HPLC Conditions

System. Waters system 9
Column. Waters symmetry C₁₈, 5μ, 150x3.9mm (SPOL 130)
Flow Rate. 1.5 ml/min
Inj Vol. 100 μl.
Temp. 35 °C
Detection. UV at 240 nm
Run Time. 35 min
Mobile Phase. RS0 [REDACTED].002.PL. RS026 pg 128

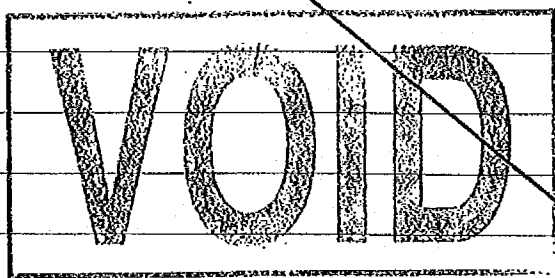
Project number

Date [REDACTED]Continued from page number 127Temp StudySystem SuitabilityStandard A (vial 2) $\Sigma = 12535253$ Standard B (vial 1; inj 2-6) $\Sigma = 12594627$ %RSD = 0.2

$$\text{Std Recovery} = \frac{12535253 \times 10.07 \times 100}{12594627 \times 10.01} = 100.1\%$$

%RSD ($n=5$) [REDACTED] (spec ≤ 0.1) [REDACTED] 0.2%Std Recovery [REDACTED] (spec 98.0-102.0) 100.1%* USP Tailing (T) (spec ≤ 2.0) [REDACTED] Epimer A $\text{PL} = 1.15$ Epimer B = 1.14* USP Resolution (R) (spec > 1.5) [REDACTED] ~~1.82~~ 1.82
PL 9 [REDACTED]Efficiency (plates) PL [REDACTED]

* Taken from Standard b (vial 1) Injection 2:

System suitability complies to requirements set
in DTMCOOR v2.PL [REDACTED]

Author signature

[Signature]

Date

[REDACTED]

Reviewer signature

[Signature]

Date

[REDACTED]

Witnessed and understood by

[Signature]

Date

[REDACTED]

Temp Study

Budesonide Content

Calculation:

$$\frac{\text{Area Sam} \times \text{Wt Std} \times \text{Vol Sam} \times P \times \text{Density}}{\text{Area Std} \times 100 \times \text{Wt Sam} \times 100}$$

$$\frac{2506882.1 \times 10.01 \times 100 \times 99.8 \times 1.004}{12572719 \times 100 \times 0.5322 \times 100} = 37.5775 \text{ mg/ml}$$

$$\frac{2506882.1 \times 10.01 \times 100 \times 99.8 \times 1.004}{12572719 \times 100 \times 0.5322 \times 100} = 37.5775 \text{ mg/ml}$$

$$\frac{2506882.1 \times 10.01 \times 100 \times 99.8 \times 1.004}{12572719 \times 100 \times 0.5322 \times 100} = 37.5775 \text{ mg/ml}$$

$$\text{Std Recovery} = \frac{\text{Actual Conc} \times 100}{\text{Theor Conc}} = \frac{37.5775 \times 100}{37.667} = 99.8\%$$

Sample Run	Sample ID	Total Budesonide	Peak Area	Sample Wt	mg/ml	Actual Wt of Conc	% Concentrate
STD A		12516482			N/A		
STD A		12554024			N/A		
A1		25068821	0.5322		37.5775	37.667	99.8
A2		25055501	0.532		37.5717	37.667	99.7
A3		24907493	0.546		36.3920	37.667	96.6
A4		23999541	0.5209		36.7551	37.667	97.6
STD A		12609951			N/A		
STD A		12610419			N/A		
A5		24186026	0.5189		37.1835	37.667	98.7
A6		25078625	0.5373		37.2354	37.667	98.9
A7		25938036	0.5498		37.6358	37.667	99.9
A8		25062187	0.5364		37.2734	37.667	99.0
STD A		12606980			N/A		
STD A		12607422			N/A		
B1		26795541	0.2847		74.9571	75.1422	99.8
B2		26831103	0.287		74.4551	75.1422	99.1
B3		25676699	0.2761		74.0645	75.1422	98.6
B4		27280923	0.2931		74.1278	75.1422	98.6
STD A		12585416			N/A		
STD A		12575839			N/A		
B5		23714967	0.2641		74.4016	75.1422	99.0
B6		25389995	0.2741		73.8445	75.1422	98.3
B7		26916021	0.2859		75.0518	75.1422	99.9
B8		25422068	0.2704		74.9495	75.1422	99.7
STD A		12581243			N/A		
STD A		12583663			N/A		
C1		23813148	0.2519		75.2784	75.0982	100.2
C2		24662048	0.2619		74.9852	75.0982	99.8
C3		24129500	0.25		76.8582	75.0982	102.3
C4		28908820	0.3005		76.6068	75.0982	102.0
STD A		12607935			N/A		
STD A		12609307			N/A		
D1		23283410	0.2502		148.1188	150.1612	98.6
D2		22258643	0.2391		148.1733	150.1612	98.7
D3		23005665	0.2466		148.4884	150.1612	98.9
D4		23902695	0.2548		149.3132	150.1612	99.4
STD A		12594370			N/A		
STD A		12600801			N/A		

Author signature

Date

Reviewer signature

Date

Witnessed and understood by

Date

P.L. N/A

Project number

Date

Continued from page number 129

Temp Study
Related Subs.
 Calc.

Known Deqs.

$$= \frac{A_{imp}}{A_{act}} \times RF \times 100.$$

A_{act}

$$RF - 16\alpha \text{ Hydro} - 0.89$$

$$- \text{Resonide} - 0.99$$

Example A1. - 16 α Hydrox

$$- 2,1\text{-Dehydro} - 1.56$$

$$= \frac{7741}{25068821} \times 0.89 \times 100 = 0.027\%$$

$$- 12\text{-Dihydro} - 0.96$$

25068821

$$- \text{Other knowns} - 1.00 *$$

* RF not calculated, taken to be 1.0.

Unknown Deqs.

$$= \frac{A_{imp}}{A_{act}} \times 100$$

A_{act}

Example A1

Inpurity at 34.0 mins (RRT = 2.13)

$$= \frac{415}{25068821} \times 100 = 0.016\%$$

25068821

VOID

P.L.

VOID

Author signature

Date

Reviewer signature

Date

Witnessed and understood by

Date

Temp Study

37 mg/ml Concentrate	Control		Heated at 110°C for 120Mins		Heated at 121°C for 20Mins		Heated at 121°C for 30Mins	
	A1	A2	A3	A4	A5	A6	A7	A8
16α Hydropredisolone	0.024	0.030	0.024	0.021	0.048	0.043	0.031	0.035
Desonide	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.
21 – Dehydro – budesonide	0.054	0.046	0.119	0.083	0.065	0.074	0.077	0.072
Budesonide – 12 – dihydro	0.017	0.018	0.021	0.020	0.019	0.020	0.020	0.021
22 – Methyl – Homologue of Budesonide	N.D.	N.D.	0.016	0.016	0.026	0.022	N.D.	N.D.
D – homobudesonide	0.022	0.022	0.020	0.019	0.021	0.020	0.021	0.021
14, 15 – dehydrobudesonide	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.
S – 11 – keto budesonide	0.017	0.022	0.030	0.032	0.025	0.023	0.025	0.025
R – 11 – keto budesonide	0.022	0.023	0.032	0.036	0.031	0.030	0.030	0.031
S – 21 – acetate budesonide	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.
R – 21 – acetate budesonide	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.
Total Known	0.054	0.00	0.119	0.083	0.065	0.074	0.077	0.072
Mean of Total Knowns	0.027		0.101		0.070		0.075	
Unknown 1 RRT 1.78	0.031	0.032	0.062	0.065	0.016	0.057	0.034	0.064
Unknown 2 RRT 2.13	0.016	N.D.	N.D.	0.013	N.D.	N.D.	N.D.	N.D.
Max Unknown RRT 1.78	0.031	0.032	0.062	0.065	0.016	0.057	0.034	0.064
Total Unknown	0.00	0.00	0.062	0.065	0.00	0.057	0.00	0.064
Mean of Total Unknowns	0.00		0.064		0.029		0.032	
Total Impurities	0.054	0.00	0.181	0.148	0.065	0.131	0.077	0.136
Mean of Total Impurities	0.027		0.164		0.098		0.107	

Void

R.

Void

Author signature

Date

Reviewer signature

Date

Witnessed and understood by

Date

P. S. M. S.

N/A R.

Temp Study

75 mg/ml Concentrate	Control		Heated at 110°C for 120Mins		Heated at 121°C for 20Mins		Heated at 121°C for 30Mins	
	B1	B2	B3	B4	B5	B6	B7	B8
16 α Hydropredisolone	0.039	0.039	0.055	0.048	0.058	0.056	0.040	0.045
Desonide	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.
21 - Dehydro - budesonide	0.026	0.026	0.042	0.060	0.025	0.029	0.070	0.065
Budesonide - 12 - dihydro	0.017	0.019	0.021	0.021	0.019	0.019	0.019	0.018
22 - Methyl - Homologue of Budesonide	0.023	0.024	0.042	0.034	0.043	0.037	0.019	0.026
D - homobudesonide	0.021	0.021	0.020	0.020	0.020	0.020	0.020	0.020
14, 15 - dehydrobudesonide	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.
S - 11 - keto budesonide	0.023	0.025	0.034	0.030	0.019	0.018	0.018	0.020
R - 11 - keto budesonide	0.029	0.029	0.033	0.035	0.043	0.024	0.024	0.024
S - 21 - acetate budesonide	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.
R - 21 - acetate budesonide	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.
Total Known	0.00	0.00	0.055	0.060	0.058	0.056	0.070	0.065
Mean of Total Knowns	0.00		0.058		0.057		0.068	
Unknown 1 RRT 1.78	0.031	0.051	0.067	0.044	0.029	0.029	0.029	0.047
Unknown 2 RRT 2.13	0.016	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.
Max Unknown RRT 1.78	0.031	0.051	0.067	0.044	0.029	0.029	0.029	0.047
Total Unknown	0.00	0.051	0.062	0.00	0.00	0.00	0.00	0.00
Mean of Total Unknowns	0.026		0.031		0.00		0.00	
Total Impurities	0.054	0.051	0.122	0.060	0.058	0.056	0.070	0.065
Mean of Total Impurities	0.053		0.091		0.057		0.068	

Void

Pl.

Void

Author signature

Date

Reviewer signature

Date

Witnessed and understood by

Date

Temp Study

75 mg/ml Concentrate	Control		Heated at 121°C for 20Mins	
	C1	C2	C3	C4
16 α Hydropredisolone	0.044	0.053	0.054	0.046
Desonide	N.D.	N.D.	N.D.	N.D.
21 - Dehydro - budesonide	0.025	0.022	0.027	0.051
Budesonide - 12 - dihydro	0.020	0.020	0.022	0.023
22 - Methyl - Homologue of Budesonide	0.027	0.039	0.040	0.035
D - homobudesonide	0.021	0.021	0.020	0.020
14, 15 - dehydrobudesonide	N.D.	N.D.	N.D.	N.D.
S - 11 - keto budesonide	0.023	0.025	0.027	0.031
R - 11 - keto budesonide	0.027	0.028	0.030	0.036
S - 21 - acetate budesonide	N.D.	N.D.	N.D.	N.D.
R - 21 - acetate budesonide	N.D.	N.D.	N.D.	N.D.
Total Known	0.00	0.053	0.054	0.051
Mean of Total Knowns	0.027		0.053	
Unknown 1 RRT 1.78	0.055	0.056	0.040	0.056
Unknown 2 RRT 2.13	N.D.	N.D.	N.D.	N.D.
Max Unknown	0.055 RRT 1.78	0.056 RRT 1.78	0.040 RRT 1.78	0.056 RRT 1.78
Total Unknown	0.055	0.056	0.00	0.056
Mean of Total Unknowns	0.056		0.028	
Total Impurities	0.055	0.109	0.054	0.107
Mean of Total Impurities	0.082		0.081	

Void

P.L.

Void

Author signature

Date

Reviewer signature

Date

Witnessed and understood by

Date

P.L.

N/A P.L.

Project number

Date

Continued from page number

153

Temp Study -

150 μ g

Concentrate	Control		Heated at 121°C for 20Mins	
	D1	D2	D3	D4
16 α Hydropredisolone	0.047	0.048	0.059	0.055
Desonide	N.D.	N.D.	N.D.	N.D.
21 - Dehydro - budesonide	0.025	0.031	0.028	0.034
Budesonide - 12 - dihydro	0.022	0.024	0.025	0.029
22 - Methyl - Homologue of Budesonide	0.031	0.031	0.047	0.040
D - homobudesonide	0.021	0.021	0.020	0.020
14, 15 - dehydrobudesonide	N.D.	N.D.	N.D.	N.D.
S - 11 - keto budesonide	0.021	0.023	0.023	0.023
R - 11 - keto budesonide	0.026	0.030	0.030	0.032
S - 21 - acetate budesonide	N.D.	N.D.	N.D.	N.D.
R - 21 - acetate budesonide	N.D.	N.D.	N.D.	N.D.
Total Known	0.00	0.00	0.059	0.055
Mean of Total Knowns	0.00		0.057	
Unknown 1 RRT 1.78	0.052	0.051	0.042	0.045
Unknown 2 RRT 2.13	N.D.	N.D.	N.D.	N.D.
Max Unknown	0.052 RRT 1.78	0.051 RRT 1.78	0.042 RRT 1.78	0.045 RRT 1.78
Total Unknown	0.052	0.051	0.042	0.045
Mean of Total Unknowns	0.052		0.044	
Total Impurities	0.052	0.051	0.059	0.055
Mean of Total Impurities	0.052		0.057	

Author signature

Date

Reviewer signature

Date

Witnessed and understood by

Date

Temp Study

	Brand
16 α Hydropredisolone	0.041
Desonide	N.D.
21 - Dehydro - budesonide	0.209
Budesonide - 12 - dihydro	0.071
22 - Methyl - Homologue of Budesonide	0.065
D - homobudesonide	N.D.
14, 15 - dehydrobudesonide	N.D.
S - 11 - keto budesonide	N.D.
R - 11 - keto budesonide	0.132
S - 21 - acetate budesonide	N.D.
R - 21 - acetate budesonide	N.D.
Total Known	0.477
Unknown 1 RRT 1.78	N.D.
Unknown 2 RRT 2.13	N.D.
Max Unknown	N.D.
Total Unknown	0.00
Total Impurities	0.477

PL. 9 Sept

Conclusion

Temperature stress produces results which indicate no degradation due to stress.

Degradant ^{PL. 9 Sept} levels are below those observed in brand product,

Archived B-04 Box 2

Author signature

PL. 9 Sept

Date

Reviewer signature

PL. 9 Sept

Date

Witnessed and understood by

Date

N/A PL. 9 Sept